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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/995,749	11/29/2001	Gerritdina Hendrika Van Geel-Schutten	BO43388-CIP	3543

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ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/995,749	Applicant(s) VAN GEEL-SCHUTTEN ET AL.	
	Examiner Manjunath N. Rao, Ph.D.	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *14-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *09/604,957* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-23 are still at issue and are present for examination. Claims 1-13 are now under consideration. Claims 14-23 remain withdrawn from consideration as being drawn to non-elected invention.

Election/Restrictions

Applicant's election with traverse of Group I, Claims 1-13 in Paper No. 9 is acknowledged. The traversal is on the ground(s) that coexamination of all of Groups I-VIII would not require independent searches and can be completed within a narrow discipline. Applicants also argue that claims 1, 12, 18 and 19 did not require a restriction and that claims 17 and 18 are substantially similar to claims 12 , 18, and 19 found in the parent case. First of all claims 1 and 12 are together in group I and are not restricted. Furthermore, it is not clear to the Examiner as to as to why claims 18 and 19 should be grouped in group I just because they are similar to claim 17. The restriction is not based on the relation between the claims or their dependency between each other. Claims have been restricted as they are drawn to independent inventions as explained in the previous Office action.

Applicants argue that as claim 17 is directed to a process of producing a glucosyltransferase and claim 18 is directed to a process of producing oligosaccharide using the protein having glucosyltransferase activity and hence are sufficiently related to be in group I. While claims 17 and 18 are directed to method of making and a method of using the product of group I, they are also considered independent inventions as explained in the previous Office action. Examiner will consider rejoining claim 17, drawn to a method making the

glucosyltransferase and claim 18 drawn to a method of using the glucosyltransferase only after claims 1-13 are in condition for allowance. Until such time, applicants arguments are not found persuasive because while the searches for some groups among the eight different groups overlap, they are not coextensive. The search for each of Groups II-VIII requires the search of subclasses unnecessary for the search of elected Group I (see previous Office action). The requirement is still deemed proper and is therefore made FINAL.

Claims 14-23 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 9.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 09/604,957, filed on 6-28-2000.

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Specification

The disclosure is objected to because of the following informalities: Applicants have deleted the description for Figure 3 in "preliminary amendment" filed on 4-2-02 and furthermore, substituted the description for figure 4 as description for figure 3. Such an action

has now provided no proper figure description for both figures 3 and 4. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-13 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 1-13 are directed to "a protein" which is drawn to a product of nature. Amending the claim to include the phrase "An isolated protein" to show the hand of man would overcome this rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4 and claims 2-3, 5-13 which depend therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 and 4 are drawn to proteins having glucosyltransferase activity and 15 contiguous amino acid fragments of the same. It is not clear to the Examiner whether the 15 amino acid fragments must also have glucosyltransferase activity or whether applicants are simply claiming any 15 amino acid fragments of the above proteins irrespective of the function.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a glucosyltransferase enzyme with SEQ ID NO:2 isolated from L.reuteri, does not reasonably provide enablement for any glucosyltransferase comprising fragments of SEQ ID NO:2 (such as 15 amino acid fragment or 100-200 amino acid fragments or specific amino acid fragments such as from amino acid position 531-1781, 972-1514 or 1515-1781, or any polypeptide that show 50-70% sequence identity to these fragments, including variants, mutants and recombinants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-13 are so broad as to encompass any glucosyltransferase that shows 50-70% amino acid sequence identity to SEQ ID NO:2 or comprise fragments of SEQ ID NO:2 (see above paragraph). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of glucosyltransferases broadly

encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of a single glucosyltransferase.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any glucosyltransferase with 50-70% amino acid sequence identity to SEQ ID NO:2 because the specification does not establish: (A) regions of the protein structure which may be modified without effecting its activity; (B) the general tolerance of glucosyltransferases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residues in any glucosyltransferase with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including glucosyltransferases with an enormous number of amino acid modifications of the glucosyltransferase of SEQ ID NOS: 2. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of glucosyltransferases having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-13 are directed to polypeptides which are 50-70% identical to SEQ ID NO:2 and fragments corresponding to portions of the sequence of SEQ ID NO:2 including variants , mutants and fragments of SEQ ID NO:2. Claims 1-13 are rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides derived from SEQ ID NO:2 including modified polypeptide sequences, modified by at least one of deletion, addition, insertion and substitution of an amino acid residue in SEQ ID NO:2 and fragments of SEQ ID NO:2 that have not been disclosed in the specification. No description has been provided of the modified polypeptide sequences encompassed by the claim. No information, beyond the

characterization of SEQ ID NO:2 has been provided by applicants which would indicate that they had possession of the claimed genus of modified polypeptides. The specification does not contain any disclosure of the structure and function of all the polypeptide sequences derived from SEQ ID NO:2, including fragments and variants within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of structures and functions. Therefore many structurally and functionally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-12 are rejected under 35 U.S.C. 102(a) as being anticipated by van Geel-Schutten (a) et al. (Med. Fac. Landbouww, Gent Univ., 2000, Vol. 65/3a :197-201) or van Geel-Schutten (b)

et al. (Appl. Environ. Microbiol., July 1999, Vol. 65(7):3008-3014). This rejection is based upon the public availability of printed publications. Claims 1-12 of the instant application are drawn to a protein having glucosyltransferase activity comprising proteins which are 50-70% identical to SEQ ID NO:2 or fragments of the same wherein amino acid at specific position corresponding to their position on SEQ ID NO:2 are changed and which can produce a glucan having 38-48% 4-linked anhydroglucose units, 17-28% 6-linked anhydroglucose units and 7-20% 4,6-linked anhydroglucose units. van Geel-Schutten (a) or (b) et al. disclose a glucosyltransferase (glucanotransferase) also known as glucansucrase isolated from *L.reuteri*. Since the enzyme is isolated from the same microorganism that is claimed by the applicants, Examiner takes the position that the enzyme disclosed in the reference and the enzyme disclosed in the instant application are the same even though the reference does not disclose the amino acid sequence. Examiner takes the position that amino acid sequence information is inherent to the proteins/enzymes and therefore the enzyme in the reference has the same sequence information as that disclosed by the applicants. Thus van Geel-Schutten (a) and (b) et al. anticipate claims 1-12 of this application as written.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, 12 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Giffard et al.

(WO 96/06173-A1, 2-29-1996). This rejection is based upon the public availability of a printed publication. Claims 1, 4, 12 and 13 of the instant application are drawn to a protein having glucosyltransferase activity comprising at least 15 contiguous amino acids of a portion of SEQ ID NO:2, i.e., amino acid positions 531-1781 (claim 1), to a protein having glucosyltransferase activity comprising at least 15 contiguous amino acids of SEQ ID NO:2 (claim 4), a protein of claim 1 which can produce a glucan having 38-48% 4-linked anhydroglucose units, 17-28% 6-linked anhydroglucose units and 7-20% 4,6-linked anhydroglucose units (claim 12) and a recombinant form of the above protein (claim 13). Giffard et al. disclose a glucosyltransferase which comprises 15 contiguous amino acids of SEQ ID NO:2 and a recombinant form of the same. Since the reference also discloses that enzyme produces soluble glucan from sucrose, Examiner takes the position that the reference enzyme is capable of producing a glucan having 38-48% 4-linked anhydroglucose units, 17-28% 6-linked anhydroglucose units and 7-20% 4,6-linked anhydroglucose units. Therefore, Giffard et al. anticipate claims 1, 4, 12-13 as written.

Since the Office does not have the facilities for examining and comparing applicants' protein with the protein of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

Claims 1-12 are rejected under 35 U.S.C. 102(b) as being anticipated by van Geel-Schutten (c) et al. (Appl. Microbiol. Biotechnol., 1998, Vol. 50:697-703). This rejection is based

upon the public availability of a printed publication. Claims 1-12 of the instant application are drawn to an isolated protein having glucosyltransferase activity and whose amino acid sequence is 50-70% identical to SEQ ID NO:2, or fragments of the same wherein amino acid at specific position corresponding to their position on SEQ ID NO:2 are changed and which can produce a glucan having 38-48% 4-linked anhydroglucose units, 17-28% 6-linked anhydroglucose units and 7-20% 4,6-linked anhydroglucose units. van Geel-Schutten (c) et al. disclose a glucosyltransferase also known as glucansucrase isolated from *L.reuteri*. Since the enzyme is isolated from the same microorganism that is claimed by the applicants, Examiner takes the position that the enzyme disclosed in the reference and the enzyme disclosed in the instant application are the same even though the reference does not disclose the amino acid sequence. Examiner also takes the position that amino acid sequence information is inherent to the proteins/enzymes and therefore the enzyme in the reference has the same sequence information as that disclosed by the applicants. Thus van Geel-Schutten (c) et al. anticipate claims 1-12 of this application as written.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over van Geel-Schutten et al. (a, b or c) as applied to claims 1-12 above, and further in view of the common

knowledge n the art of protein purification, sequencing and molecular cloning. The reference of van Geel Schutten (a, b or c) as it applied to claim s 1-12 drawn to an isolated and purified glucosyltransferase isolated from *L.reuteri* has been discussed above.

With the purified enzymes provided by van Geel Schutten et al. it would have been obvious to one of ordinary skill in the art to make a recombinant enzyme of the same by using any one of the number of methods available in the art to purify the enzyme, analyze the amino acid sequence and design appropriate probes to obtain a cDNA encoding the above enzyme. Using such a cDNA to transform a host cell and culture the same, one of ordinary skill in the art would arrive at a recombinant form of the above enzyme. One of ordinary skill in the art would be motivated to do so in order to make the enzyme in large quantities in view of its use for making glucans, which have great demand in the food industry. One of ordinary skill in the art would have a reasonable expectation of success since van Geel Schutten et al. (a, b or c) teach a useful enzyme and the art provides the methods for making recombinant proteins.

Therefore, the above invention would have been *prima facie* obvious to one of ordinary skill in the art.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m..

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.

MANJUNATH RAO
PATENT EXAMINER

Manjunath N. Rao
October 11, 2002